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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/008,062	10/19/2001	David Rizzieri	5405-252	5735

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 03/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/008,062	RIZZIERI ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/22/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 22, 2005 has been entered.

2. Claims 1-6 and 8-24 are pending.

Claims 1 and 10 have been amended.

Claims 23 and 24 have been added.

Claims 1-6 and 8-24 are examined on the merits.

Maintained Rejections

Claim Rejections - 35 USC § 112

3. The rejection of claims 4, 12-22 and newly added claim 24 under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials is maintained and newly made.

Applicants assert, "the present invention is directed to the new use of a known compound.", see page 6, first full paragraph of Remarks submitted December 8, 2005. Applicants also aver the ^{131}I-labeled chimeric 81C6 monoclonal antibody was described in U.S. Patent No. 5,624,659 and the patent file reveal the antibody's sequence. These points of view and arguments have been considered, but found unpersuasive.

Applicants are reminded "The mere reference to a deposit or the biological material itself in any document or publication does not necessarily mean that the deposited biological material is readily available. ***Even a deposit made under the Budapest Treaty and referenced in a United States*** or foreign ***patent document*** would not necessarily meet the test for known and readily available unless the deposit was made under conditions that are consistent with those specified in these rules, including the provision that requires, with one possible exception (37 CFR 1.808(b)), that all restrictions on the accessibility be irrevocably removed by the applicant upon the granting of the patent. *Ex parte Hildebrand*, 15 USPQ2d 1662 (Bd. Pat. App. & Int. 1990).", see MPEP 2404.01.

The assurances must be met and made in the instant application. And while Applicants have noted they have reviewed U.S. Patent number 5,624,659. Applicants have not presented proof or evidence that the assurances made during the issuance of patent '659 are still pending. At this point in prosecution clear and sufficient evidence is not of record and the instant rejection is made and maintained.

Claim Rejections - 35 USC § 103

4. The rejection of claims 1-6, 8-22 and newly added claims 23 and 24 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent number 5,624,659 (April 29, 1997/ reference 1 from IDS submitted June 14, 2002), and in view of Rizzieri et al. (Blood 94(10), Part 2, Supplement 1: 4339, Abstract #4339 November 1999/ reference 3 from IDS submitted June 14, 2003) is maintained and newly made.

Applicants assert their claimed method yields unexpected results, which were previously submitted in a 1.132 declaration by Dr. Rizzieri on October 5, 2004. Applicants note these unexpected results are

(1) the rapid uptake of ^{131}I anti-tenascin chimeric 81C6 monoclonal antibody in the liver and marrow and a slower and enhanced uptake in selected tumor sites opposed to normal organs;

(2) at least a 2-fold greater retention of the radiolabeled antibody in lymphomas as compared to normal tissue;

(3) the estimated average absorbed dose to selected tumors of ^{131}I anti-tenascin chimeric 81C6 monoclonal antibody was higher than that obtained from ^{131}I-tositumomab; and

(4) the instant radiation dose delivered to the tumor per unit administered activity was higher than seen with ^{131}I-tositumomab and consequently these results indicate substantially longer tumor retention than reported for other antibodies evaluated for radioimmunotherapy. These arguments and points of view have been carefully reviewed and considered, but found unpersuasive.

The arguments are not fully commensurate in scope with the claims. Most of the claims read on the treatment of lymphoma with any antibody coupled to any radioisotope. And assuming *arguendo* that the arguments were fully commensurate, the comparison between ^{131}I anti-tenascin chimeric 81C6 monoclonal antibody and ^{131}I-tositumomab is not effective in substantiating a supposed unexpected result of treating with ^{131}I anti-tenascin chimeric 81C6 monoclonal antibody. The two ^{131}I antibodies recognize two different antigens, ^{131}I anti-tenascin chimeric 81C6 monoclonal antibody recognizing tenascin and ^{131}I-tositumomab recognizing CD20, therefore there are differences in the antibodies' absorption rate, affinity to targets, as well as tumoricidal activity.

Applicants attempt to substantiate supposedly unexpected results by comparing the longer tumor retention rate of ^{131}I anti-tenascin chimeric 81C6 monoclonal antibody against other radioimmununotherapy (RAIT) antibodies, such as anti-CEA hMN-14, anti-TAG72 CC49, A33 and 17-1A, see page 8, last paragraph of Remarks. All of the other antibodies listed bind targets on solid tumors. Carcinoembryonic antigen (CEA) is expressed in a wide variety of adenocarcinomas, such as colon, rectum, pancreas, gastric and breast. Both, anti-TAG72 CC49 and 17-1A recognize antigens on colorectal carcinomas and A33 recognizes targets on esophageal squamous cancers. The art teaches "solid tumors are radioresistant unlike hematologic tumors whose radiosensitivity is in part due to the ease with which lymphoid cells undergo apoptois at relatively low absorbed radiation doses.", see Govindan et al. (Technology in Cancer Research and Treatment 4(4): 375-391, August 2005. Assumed unexpected results

predicated upon antibodies that are structurally different and bind distinct target antigens do not represent persuasive data or evidence.

It continues to stand that a proper and formidable *prima facie* case of obviousness was established in paragraph 7 of the first action on the merits (FAOM) mailed July 7, 2004 meeting the three basic criteria of a rejection under 35 U.S.C. 103(a). The radiolabeled chimeric monoclonal antibody, ^{131}I -81C6 or therapeutic antibodies (dosage to the patient in the range of 10mCi to 100mCi) of the disclosed invention are used in the treatment of any tumor that expresses tenascin, see patent, column 2, lines 40-49; bridging paragraph of columns 2 and 3; column 3, line 20-column 4, line 44. And Rizzieri notes non-Hodgkin's lymphomas have increased angiogenesis and microvessel density (MVD) and consequently increased expression of tenascin, see Rizzieri abstract, particulary the last paragraph. Rizzieri plainly "...suggests systemically delivered anti-tenascin antibody may be an effective form of therapy." Intrinsically, the taught method would provide for at least a two-fold greater retention of the antibody in the lymphoma given all the reagents are the same and the motivation to utilize them is clearly present in the references. Based on the combination of these reference teachings one of ordinary skill in the art would have arrived at the claim invention at the time with a reasonable expectation of success. Both references provide suggestion and motivation to establish and arrive at the claimed invention, accordingly the rejection is maintained.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571) 272-0831. The Examiner works a flexible schedule, however she can normally be reached between the hours of 7:30 am to 6:30 pm with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
01 March 2006